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Automatic comparison of stimulus durations in the primate prefrontal cortex: the neural basis of across-task interference

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1Department of Physiology and Pharmacology, Sapienza University of Rome, Rome, Italy; 2Department of Intelligence Science and Technology, Graduate School of Informatics, Kyoto University, Kyoto, Japan; 3Nielsen Neuro, Tokyo, Japan; and 4Olszewski Institute for the Neurobiology of Knowledge, Potomac, Maryland and Edmond and Lily Safra International Institute of Neurosciences of Natal, Natal, Brazil

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Genovesio A, Cirillo R, Tsujimoto S, Mohammad Abdellatif S, Wise SP. Automatic comparison of stimulus durations in the primate prefrontal cortex: the neural basis of across-task interference. J Neurophysiol 114: 48–56, 2015. First published April 22, 2015; doi:10.1152/jn.00057.2015.—Rhesus monkeys performed two tasks, both requiring a choice between a red square and a blue circle. In the duration task, the two stimuli appeared sequentially on each trial, for varying durations, and, later, during the choice phase of the task, the monkeys needed to choose the one that had lasted longer. In the matching-to-sample task, one of the two stimuli appeared twice as a sample, with durations matching those in the duration task, and the monkey needed to choose that stimulus during the choice phase. Although stimulus duration was irrelevant in the matching-to-sample task, the monkeys made twice as many errors when the second stimulus was shorter. This across-task interference supports an order-dependent model of the monkeys’ choice and reveals something about their strategy in the duration task. The monkeys tended to choose the second stimulus when its duration exceeded the first and to choose the alternative stimulus otherwise. For the duration task, this strategy obviated the need to store stimulus-duration conjunctions for both stimuli, but it generated errors on the matching-to-sample task. We examined duration coding in prefrontal neurons and confirmed that a population of cells encoded relative duration during the matching-to-sample task, as expected from the order-dependent errors.

METHODS

Two monkeys (Macaca mulatta), males weighing 8.0–8.5 kg, served as subjects in this study. All procedures were approved in advance by the National Institute of Mental Health Animal Care and Use Committee. The monkeys were seated in a primate restraint chair with heads fixed and their eyes 29 cm away from a video monitor.
Three 3 × 2 cm switches were located under the video monitor and within reach. They were arranged left to right, with a 7 cm center-to-center separation. The fixation spot was a 0.6° filled white circle, which always appeared at the center of the monitor and had to be fixated visually within ± 7.4°. The two discriminant stimuli were a filled 3°-diameter blue circle and a filled 3°×3° red square. Although the stimuli differed in both color and shape, for convenience we refer to them only in terms of their color for the remainder of this report.

**Tasks.** The monkeys began each trial by touching the central key with their left hands. Upon contact with the switch, the fixation spot appeared at the center of the video monitor. After a fixation period of either 400 or 800 ms, the two discriminant stimuli appeared in a sequence, which differed by task.

For the duration-discrimination task (Fig. 1A), the blue circle and the red square appeared on each trial in succession at the location of (and occluding) the fixation point. The two stimuli appeared in either order, red-blue or blue-red, separated by a variable delay period in which the fixation point was again visible. The first stimulus was called S1, and it lasted 200–1,200 ms. The S1 stimulus was followed by the first delay period, called D1 (400–800 ms). In a subset of sessions, a D1 period of 1,200 ms was also used, and in yet other sessions a fixed 1,200 ms D1 period replaced the variable ones.

After the end of the D1 period, the second stimulus appeared for 200–1,200 ms. We called this stimulus event S2. After S2, a second delay period, called D2, lasted either 0, 400, or 800 ms. The D2 period thus began at S2 offset and ended at the time of the “go” signal, which consisted of the red and blue stimuli reappearing, one to the left of the fixation point and the other to the right, pseudorandomly determined. The duration of S1 and S2 always differed, and both were selected randomly from a set of stimulus durations ranging from 200 ms to 1,200 ms in steps of 200 ms. The “go” signal ended the fixation requirement. To receive a reward, the monkeys had to touch the switch below the stimulus that had lasted longer on that trial; otherwise, the trial terminated without any reward. The monkeys had a time limit of 6 s to touch a switch, but in practice both monkeys did so in <500 ms.

In the matching-to-sample task (Fig. 1B), S1 and S2 were always the same stimulus, either blue or red. Accordingly, the monkeys could not compare durations of blue and red stimuli, as they did in the duration task. Otherwise, the events and intervals matched those in the duration task, including the durations of the S1, D1, S2, and D2 periods, the “go” signal, the stimulus locations, and the fixation requirement. To receive a reward, the monkeys had to touch the switch below the choice stimulus that had appeared twice on a given trial. Each trial had an equal probability of having a blue or red sample stimulus, and so chance-level performance was 50% correct.

In both tasks, acoustic feedback signaled an error, and an intertrial interval of 700–1,000 ms followed all trials. The two tasks were run in consecutive blocks with no fixed order.

**Surgery.** The monkeys underwent surgery with aseptic techniques and isoflurane anesthesia (1–3%, to effect). We implanted recording chambers over the exposed dura mater of the left frontal lobe, along with head restraint devices, monkey 1 had two 18 mm diameter chambers, implanted at different times during the experiment, and monkey 2 had a single 27 × 36 mm chamber.

**Data collection.** An infrared oculometer recorded eye position (Arrington recording, Scottsdale, AZ), and quartz-insulated platinum-iridium electrodes (0.5–1.5 MΩ at 1 kHz) recorded single-cell activity. A 16 electrode drive assembly (Thomas Recording, Giessen, Germany) positioned the microelectrodes, which were arrayed in a concentric pattern with 518 µm spacing. We discriminated single-unit potentials online using the Multichannel Acquisition Processor, each of which was confirmed with the Offline Sorter (Plexon, Dallas, TX). The latter used principal component analysis, minimal interspike intervals, and clearly differentiated waveforms inspected individually for every isolated neuron. The analyses were performed by using the MATOFF software (Genovesio and Mitz 2007).

**Neurophysiological analysis.** Previous reports used the same neuronal dataset (Genovesio et al. 2009, 2012). The present analysis focused on three periods: the decision period, the D2 period, and the reaction and movement time period (RMT). The decision period was defined as an interval of 80–400 ms after the ideal decision point, which refers to the instant that an ideal observer could have made a decision. The duration task had two decision points, depending on whether S1 was longer than S2. If S1 was longer, then an observer could decide whether the red or blue stimulus had lasted longer at the time of S2 offset. Otherwise, a decision could be made once the duration of S2 surpassed that of S1. In the matching-to-sample task, the monkeys made a decision as soon as S1 appeared, but to make a comparison between tasks as comparable as possible, we treated the data from the matching-to-sample task exactly like those from the duration task. The RMT period corresponded to the interval between the “go” cue and the report (touching either the left or right switch). In both tasks, relative duration coding was assessed in these three periods with a one-way ANOVA.

Because the number of trials in the duration task (a mean of 190) exceeded that in the matching-to-sample task (a mean of 88), we reduced the number of trials in the duration task for each session to match the number of trials in the matching-to-sample task. To do that, we adopted two methods. One method consisted of eliminating later trials from the duration task, retaining the first n trials, where n is the number of trials obtained for the matching-to-sample task. For three cells, we had more trials in the matching-to-sample task, so we eliminated the later trials from that task, instead. The second method consisted of randomly selecting trials in the task with more trials to match the number obtained for the other task, performing the analysis 1,000 times for each session.

To compare the magnitude of relative duration coding in terms of the order of stimuli, we calculated activity (A) differences for each pair of task: ΔA2 − ΔA1, where ΔA2 was the average discharge rate on trials when S2 was longer than S1, and ΔA1 was the average rate when S1 was longer. Analogous differences were calculated for the matching-to-sample task, even though S1 and S2 were the same stimuli in terms of color and shape. We also calculated the normalized preference indices in the form of a contrast ratio: (ΔA2 − A1)/(ΔA2 + A1).

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**Fig. 1.** Sequence of task events. Each gray rectangle represents the video screen. A: duration task. In this example trial, the first blue stimulus lasted longer than the 2nd red stimulus. Therefore when the 2 stimuli reappeared on the screen with the blue stimulus to the left and the red stimulus to the right, the correct choice was to press the left switch, as illustrated by the monkey’s hand moving to the left. B: matching-to-sample task. In this example trial, the blue stimulus was presented twice, and the correct choice was to press the left switch corresponding to the blue goal. C: penetration sites for both monkeys. The blue line divides the dorsolateral PF area (anterior) from the periarcuate area (posterior). Abbreviations: AS, arcuate sulcus; D1, first delay period; D2 second delay period; PS, principal sulcus; S1, first stimulus; S2 second stimulus.
Histological analysis. Ten days prior to perfusing the monkeys with formal saline, we made electrolytic marking lesions (15 μA for 10 s). We plotted recording sites on frontal sections, stained for Nissl substance, using the recovered marking lesions and pins inserted during the perfusion as the reference points. We also used structural magnetic resonance images obtained at various times during the recording procedures. Although the entry points for more posterior recordings (Fig. 1C) make it appear that many cells were located in the postarcuate cortex, reconstructions of the recording sites that take into account both the angle and depth of penetrations indicated that nearly all of the recorded cells were located either in the prearcuate cortex, which corresponds to area 8, or more rostrally in area 46.

RESULTS

Behavior. We tested two models of decision making, which we call the order-independent (OI) model and the order-dependent (OD) model. For simplicity, we will describe these models in terms of stimulus color, although the shape dimension could have served, as well.

The OI model (Fig. 2, A and B) assumes that the durations of the blue and the red stimuli are both encoded and stored and that these durations are compared either during or after the presentation of S2. Consider, for example, a trial in which S1 is red and S2 is blue. According to the OI model, a subsequent comparison requires encoding the duration of the red S1, which is maintained in memory as a feature-duration conjunction over the delay between the two stimuli (Fig. 2, A and B). During or after the presentation of the blue S2, a comparison is made between the remembered duration of the red S1 and the duration of the blue S2.

The OD model (Fig. 2, C and D), in contrast, assumes that the duration of S1 and S2 are compared with no need to maintain the duration of the color-S1 conjunction in memory. Specifically, this model assumes that while the duration of S1 is stored in short-term memory, its color is not. The OD model assumes further that, during or after the presentation of S2, the durations of S1 and S2 are compared in an initial computational step that is independent of color. Then, in a second step, it would be sufficient to apply a simple rule to solve the problem posed by the task: note the color of S2, and if S2 lasts longer than S1, then choose S2’s color as the next goal (Fig. 2C); if not, choose the alternative color (Fig. 2D). The OD model is color-independent, at least initially, in the sense that it does not require a duration-color conjunction to be maintained in memory during the D1 period and requires instead a comparison based solely on the remembered duration of S1, independent of its sensory features. The order dependence of the model follows from the fact that it is the duration of the S1 that must be maintained in memory during the delay period between the first and second stimulus: the D1 period.

Fig. 2. A, B: order-independent (OI) model. A: when the blue stimulus is longer, the duration comparator’s output produces a choice of the blue goal. B: alternatively, when the red stimulus is longer, the comparator’s output produces the choice of the red goal. C, D: order-dependent (OD) model. C: in this example, S2 is blue and the comparator’s output is S2 longer. Subsequent application of the rule “if S2 is longer then choose its color as the goal” leads to a choice of the blue goal. D: alternatively, when S2 is shorter, the rule “if S2 is shorter then choose the alternative color as the goal” leads to a choice of the red goal.

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We tested whether there was a difference in performance based on which stimulus, S1 or S2, was the longest in the matching-to-sample task. Assuming that a proportion of errors in the matching-to-sample task reflects interference from strategies employed in the duration task, the OD model predicts a greater number of errors in the matching-to-sample task when S2 is shorter. Other errors presumably reflect misperceiving or forgetting the stimuli, followed by a random choice among the two options. When S2 is longer, the OD model predicts that S2 will be selected as the goal, which would generate the correct choice in the matching-to-sample task, as it would (by design) in the duration task. When S2 is shorter, however, the OD model would produce the correct choice in the duration task, but this strategy would interfere with making the correct choice in the matching-to-sample task. Avoiding the shorter S2 stimulus during the choice phase would lead to a choice of the nonmatching test stimulus, in violation of the matching-to-sample rule.

Figure 3, A and B, shows that, on the duration task, the monkeys made approximately the same proportion of errors when S2 was shorter as when S2 was longer. Table 1 gives the numbers of errors and trials. No differences were significant on this task, for either monkey 1 (binomial test, \( P = 1.00 \)) or monkey 2 (binomial test, \( P = 0.067 \)). In contrast, on the matching-to-sample task, both monkeys made approximately twice as many errors when S2 was shorter than when S2 was longer (Fig. 3B), a difference that was highly significant for both monkeys (binomial test, \( P < 0.001 \)).

**Encoding of relative duration in the duration and matching task.** The neural sample consisted of 342 cells recorded in both tasks. Of these cells, 257 cells were recorded in the caudal PF cortex (PFc) and 85 cells were recorded from dorsolateral prefrontal PF cortex (PFdl). Table 2 shows the results of a one-way ANOVA on activity during the decision and the D2 periods, with relative duration as the factor, divided by area and task period. During the D2 period, neurons were selective for the relative duration both in the duration task (91/342, 27\%) and in the matching-to-sample task (42/342, 12\%). Similar results were found for the decision period (see METHODS for the definition of this interval). Later in each trial, during the RMT period, neurons encoded relative duration less frequently, for both the duration task (42/342, 12\%) and the matching-to-sample task (25/342, 7\%). Accordingly, we did not conduct any further analysis on the RMT period.

Table 3 shows the results from a one-way ANOVA repeated 1,000 times for each cell on the trials obtained from 1,000 reductions of the task with more trials, with random trial selection (see METHODS). This analysis confirms the results found after the alternative trial-reduction method, which was

![Figure 3](https://example.com/figure3.png)

**Figure 3.** A: ratio of number of errors between S2-shorter trials and S2-longer trials. B: percentage of errors in the duration and matching-to-sample task, divided by monkey and by which stimulus was shorter, S1 or S2. C, D: cells with a significant relative duration effect. The Venn diagram shows the number of cells with significant effects in the D2 period (C) and in the decision period (D). The shaded background represents the cells encoding the relative duration in both tasks. Percentages refer to the total number of cells significant by 1-way ANOVA in either one or both tasks. MTS, matching-to-sample task.

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**Table 1. Number and percentages of error trials divided by S2 longer and shorter trials**

<table>
<thead>
<tr>
<th>Task</th>
<th>Task Monkey</th>
<th>Errors S2 Shorter</th>
<th>Errors S2 Longer</th>
<th>Total Trials S2 Shorter</th>
<th>Total Trials S2 Longer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>monkey 1</td>
<td>62 (20%)</td>
<td>61 (20%)</td>
<td>305</td>
<td>309</td>
</tr>
<tr>
<td></td>
<td>monkey 2</td>
<td>868 (19%)</td>
<td>947 (20%)</td>
<td>4,638</td>
<td>4,788</td>
</tr>
<tr>
<td>Matching-to-sample</td>
<td>monkey 1</td>
<td>91 (24%)</td>
<td>44 (12%)</td>
<td>382</td>
<td>361</td>
</tr>
<tr>
<td></td>
<td>monkey 2</td>
<td>372 (9%)</td>
<td>186 (5%)</td>
<td>4,005</td>
<td>4,156</td>
</tr>
</tbody>
</table>

The percentage of errors is calculated on the total number of trials of each type. S2, 2nd stimulus.

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**Table 2. Number of cells significant by one-way ANOVA for relative duration, divided by task and brain area**

<table>
<thead>
<tr>
<th>Task Period</th>
<th>Task</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2 delay period</td>
<td>duration</td>
<td>PFdl (85)</td>
</tr>
<tr>
<td></td>
<td>MTS</td>
<td></td>
</tr>
<tr>
<td>Decision period</td>
<td>duration</td>
<td>23 (27%)</td>
</tr>
<tr>
<td></td>
<td>MTS</td>
<td>16 (19%)</td>
</tr>
</tbody>
</table>

PFdl, dorsolateral prefrontal cortex; PFc, caudal prefrontal cortex; D2, 2nd delay period; MTS, matching-to-sample task.
Both, the cells significant in both tasks; duration and MTS, number of cells includes also the “both” cells.

used to classify neurons. In this method, later trials were eliminated to match trial numbers from task to task.

Figure 3, C and D, shows that there were, in addition to neurons encoding the relative duration in both tasks, neurons modulated by stimulus duration only in the matching-to-sample task and only in the duration task. Figure 4, A and B, shows two example cells that encoded the relative duration specifically in one task.

Table 3. Number of cells significant by one-way ANOVA for relative duration, divided by task after 1,000 trial reductions of the task with more trials, with random trial selection

<table>
<thead>
<tr>
<th>Task period</th>
<th>Task</th>
<th>Mean of Reductions, ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2 duration</td>
<td>MTS</td>
<td>81 ± 6</td>
</tr>
<tr>
<td>D2 duration</td>
<td>both</td>
<td>41 ± 0.4</td>
</tr>
<tr>
<td>D2 duration</td>
<td>both</td>
<td>12 ± 2</td>
</tr>
<tr>
<td>Decision period</td>
<td>duration</td>
<td>86 ± 5</td>
</tr>
<tr>
<td>Decision period</td>
<td>MTS</td>
<td>57 ± 0.2</td>
</tr>
<tr>
<td>Decision period</td>
<td>both</td>
<td>31 ± 2</td>
</tr>
</tbody>
</table>

Figure 4A shows a cell encoding relative duration only in the duration task. During the delay period, it had higher activity when S2 was shorter than when S2 was longer. The same neuron had the same activity level for both durations in the matching-to-sample task. Figure 4B shows another neuron, which had the opposite properties. This cell encoded relative duration only in the matching-to-sample task, with higher activity when S2 was shorter.

Figure 5 plots an index of relative duration coding for the matching-to-sample task against an index of duration coding for the duration task in both the decision period (Fig. 5A) and the D2 delay period (Fig. 5B). The cells selective for both tasks (red circles) had the same preference in both tasks, with only one exception (Fig. 5B, lower right quadrant). We also took into account the fact that cells with selective relative-duration coding for the matching-to-sample task, by statistical analysis (green circles), nevertheless had a nonzero duration-coding index in the duration task (Fig. 5, A and B). These values failed to reach statistical significance based on ANOVA, but even considering these nonsignificant results, only a few cells had different preferences in the two tasks. Figure 5B shows one clear example in the upper left quadrant and one in the lower right quadrant.

Table 4 contrasts relative-duration coding for correct and error trials during the matching-to-sample task. In the decision period, these indexes were significantly higher for error trials in two classes of cells: those that encoded relative duration only in the duration task and those that did so in both tasks. In the D2 period, there was a significant difference only for cells that showed relative-duration coding selectively in the duration task. No difference was found for the cells encoding relative duration only in the matching-to-sample task, for either the D2

![Fig. 4. Neurons encoding relative duration. Raster displays spike (sp) times beneath spike-density averages. A: activity of a neuron encoding significantly the relative duration (1-way ANOVA, \(P = 0.0000\)) with higher activity in the D2 period for S1-longer trials in the duration task but not in the matching-to-sample task. Rasters are aligned on S2 offset. The light gray background indicates the delay period. B: activity of a neuron with a significant higher activity (1-way ANOVA, \(P = 0.0049\)) in S1-longer trials in the D2 period only in matching-to-sample task but not in the duration task. The squares on the right side of S2 offset represent the “go” signal, which corresponds to the appearance of the 2 potential choice stimuli.](http://jn.physiology.org/)

![Fig. 5. A, B: comparison of the modulation indexes in the matching-to-sample and the duration tasks. Cells significantly modulated by relative duration, by 1-way ANOVA, only in the duration task (blue), only in the matching-to-sample task (green), or in both tasks (red). A: decision period. B: D2, 2nd delay. MTS, matching-to-sample task.](http://jn.physiology.org/)
or decision periods. This finding suggests that the relative-duration signal generating the interference was limited to cells encoding relative duration in both tasks or only in the duration task.

We also examined whether our findings could result from differences in task difficulty. It has been reported that PF cells are more active in the more difficult of two tasks, as predicted by the multiple-demand theory of PF function (Duncan 2010). Lennert and Martinez-Trujillo (2011), for example, found higher levels of activity in a color-rank task compared with a simple fixation control task. Perhaps, in this present experiment, more cells encoded relative duration in the duration task because of a general reduction of activity during the matching-to-sample task. To test this idea, we calculated the mean firing rate for the two tasks. There was no significant difference between the matching-to-sample [D2 delay = 11.2 ± 11.1 (SD) spikes/s; decision = 11.3 ± 11.05 spikes/s] and duration [D2 delay = 10.5 ± 10.9 (SD) spikes/s; decision = 11.0 ± 11.4 spikes/s] tasks, either in the D2 delay period (paired t-test, \( P = 0.14 \)) or in the decision period (\( P = 0.42 \)).

We further quantified the population selectivity of the three categories of cells by a receiver operating characteristic (ROC) analysis. Figure 6, A and B, shows the results for the D2 period and the decision period. As expected, neurons that the ANOVA classified as encoding relative duration specifically in the matching-to-sample task had a higher ROC value in that task than in the duration task in both D2 and decision periods (Kruskal-Wallis test, \( P < 0.001 \)). Although fewer in number, the only MTS cells encoding the relative duration in the matching-to-sample task did not differ significantly in their degree of selectivity from the only duration cells in the duration task in the D2 period (Kruskal-Wallis test, \( P = 0.10 \)). The same result was obtained for the decision period (\( P = 0.15 \)). For cells encoding relative duration in both tasks, there was a significant task-to-task difference in the decision period (\( P = 0.03 \)) but not in the D2 period (\( P = 0.29 \)).

We tested whether the relative duration coding in the matching-to-sample task was dependent on how long it had been since the monkeys switched from the duration task. For example, we explored whether relative-duration coding was more pronounced at the beginning of a block of trials in the matching-to-sample task than at its end. We calculated ROC values in the first five and last five trials in each block of matching-to-sample trials. In the D2 period, the average ROC value for the first five trials (0.631) did not differ from that for the last five (0.639), ruling out a carry-over effect from a previous task or a dissipation of the relative-duration signal as matching-to-sample trials accumulated.

### DISCUSSION

We found that a strategy used in the duration task produced across-task interference with the matching-to-sample performance, which supports a decision model for the duration task based on stimulus order. Our results also show that the PF encodes relative duration during the matching-to-sample task. We take up these two findings, in turn, followed by a consideration of mechanisms for reducing interference through mutual inhibition.

**OD decision-making.** Although the monkeys performed the matching-to-sample task well above the chance level of 50% correct, we found that their errors depended disproportionately on the relative durations of S1 and S2. Specifically, the monkeys tended to choose S2 when it was longer but avoid it when it was shorter. This strategy produced errors on the matching-to-sample task, which added to errors resulting from the misperception or forgetting of the stimuli.

We compared two models of decision making for the duration task, the OI and the OD models, by analyzing the pattern of errors in the matching-to-sample task. The two models make different predictions on the pattern of errors in the matching-to-sample task. The OD model is based on the hypothesis that
the duration task is performed without using the information about S1’s color or any association between the S1’s color and its duration. According to this model, a stimulus comparison is performed by using two types of information: which stimulus (S1 or S2) was the longest and S2’s color (Fig. 2, C and D). The decision, according to this model, is made in two steps: assessing whether S2 is longer than S1 and then applying a simple rule: choose the S2’s color when S2 is longer and choose the alternative color when S2 is shorter. By applying this rule, there would be no need to maintain either S1’s color or the conjunction of its color and duration in memory during the D1 period. This model requires only the maintenance in memory of the duration of S1. It can be applied to the duration task because there were only two stimuli as potential choices, a red square and a blue circle. Accordingly, through the process of elimination, S2’s color was all the information needed to make a choice. This model predicts more errors on the matching-to-sample task when S2 is shorter because the application of this rule would produce the choice of the nonmatching stimulus. In contrast, the OD model (Fig. 2, A and B) predicts a decision process based on comparing the duration of the red and blue stimuli, with one of these conjunctions maintained in memory over the D1 period. This model predicts no difference in the number of errors when S2 is longer versus when it is shorter. Our results clearly support the OD model. Although the OD model can explain the difference in performance between the two trials types, it cannot explain the errors made in the S2-longer trials. These errors depend on factors not examined in this study.

Two additional considerations support the OD model. One is the observation that neurons in PF represent relative duration in the duration task (Genovesio et al. 2009). The other is that during error trials PF neurons lose their modulation for the relative information based on order (Genovesio et al. 2009). The OD model, however, does not exclude the OI model, and some PF neurons could function also as predicted by the OI model in the duration task, in a complementary way. It is possible that neurons encoding whether the red or blue stimulus lasted longer encoded the goal directly or contributed to the transformation of order-based information into a prospective code for the goal (Genovesio et al. 2012; Genovesio and Tsujimoto 2014). In contrast to this kind of domain-independent goal encoding, we have previously shown that the encoding of relative duration based on order was domain-dependent for duration and distance (Genovesio et al. 2012), with no tendency to share the same preference (see Fig. 2A in Genovesio et al. 2012; Genovesio et al. 2014a). Future studies might examine whether the same conclusion would apply to the representation of other cognitive domains, such as number or other metrics.

Coding “irrelevant” information. At the neural level, encoding of relative-duration was observed in the matching-to-sample task, in which no duration comparison was required. Given the strategy revealed by the behavioral error analysis (Fig. 3, A and B), this result confirms the use of relative-duration coding during the matching-to-sample task. Some cells encoded relative duration only in the matching-to-sample task or in both tasks (Fig. 3, C and D). Any cell encoding relative duration during the matching-to-sample task could contribute to the errors that reflect across-task interference. This includes cells that, based on correct-trial activity, were classified as showing relative-duration coding selectively during the duration task (Only Duration in Fig. 5). Contrary to this classification, this population of cells showed a high level of relative-duration coding during error trials (Table 4).

Previous neurophysiological studies have shown that irrelevant information can be represented in PF in terms of stimulus features such as color (Lauwereyns et al. 2001), motion direction (Hussar and Pasternak 2009, 2012; Lauwereyns et al. 2001), and number of stimuli (Kim et al. 2008), but the present example represents a special case. In our experiment, relative duration should have been irrelevant to performing the matching-to-sample task, but the error analysis shows that the monkeys used this information in generating their choices. Thus it appears that, like several previous studies (Genovesio et al. 2006a; Kim et al. 2008; Lauwereyns et al. 2001; Mann et al. 1988; Tsujimoto et al. 2012), the encoding of an irrelevant stimulus dimension was the consequence of the training and practice with another task.

This need not always to be the case, however, because other studies have shown that for certain information, at least, the coding of irrelevant information can emerge autonomously. Genovesio et al. (2014b), for example, showed that the previous goal could be encoded even when irrelevant for task performance. Likewise, Qi et al. (2012) showed that irrelevant information can modulate the neural activity even before training.

The present results differ from those in previous studies in another respect as well. Encoding relative duration requires a comparison process between two stimuli separated in time. Most studies of irrelevant information instead involve the coding of the sensory properties of a single stimulus.

Reduction of interference. Although speculative, it is possible that some PF neurons, in particular those neurons active only in the matching-to-sample task, function to reduce across-task interference instead of being responsible for it. This hypothesis is in line with the result that the cells of this group were the only ones that did not show higher relative-duration encoding during error trials. It is possible that irrelevant information might be suppressed by mutual inhibition of conflicting representations as in extrastriate visual areas (for a review, see Desimone and Duncan 1995; Reynolds and Heeger 2009). In the context of working memory tasks, irrelevant information in working memory can inhibit target selection as a “template for rejection” (Woodman and Luck 2007) and suppress visual processing in visual areas (Peters et al. 2012). Matsushima and Tanaka (2012) have shown that neurons modulated by irrelevant information could play an active role in the elimination of interference.

A role of PF in the reduction of interference has emerged from studies in monkeys which showed that previous choices could interfere with the current choice after PF was lesioned or disturbed (Diamond and Goldman-Rakic 1989; Tsujimoto and Postle 2012). Monkeys with PFdl lesions choose the correct location more often than chance when it matched the location two trials back (Diamond and Goldman-Rakic 1989), perhaps reflecting interference from previous trials and the absence of PF-mediated mitigation of this interference. This finding indicates an impairment in the memory of stimulus order, which is also consistent with impairments on an oculomotor delayed-response task after dysfunction of PFdl (Tsujimoto and Postle 2012). The segregation between the representation of future and previous goals could also reflect the reduction of interference (Genovesio et al. 2006b; Genovesio and Wise 2008; Genovesio and Ferraina 2014).
In this context, it is possible that some neurons encoding relative duration in the matching-to-sample task could, like the neurons described by Matsushima and Tanaka (2012), contribute to mitigating the interference effects arising from the strategies used in the duration task. Assuming, as Kusunoki et al. (2010) have proposed, a mutual inhibition (Machens et al. 2005) or opponent model of goal choice, it is to be expected that PF neurons should encode nongoal stimuli, be they distractors or stimuli rejected as goals by a task rule. For example, Hasegawa et al. (2004), in an oculomotor delayed nonmatching-to-sample task, identified a “don’t look” category of neurons activated specifically by the incorrect stimulus location. In our matching-to-sample task, a “don’t choose” population analogous to “don’t look” neurons could counter the choice of the alternative stimulus, the stimulus other than S2, on trials when the S2 stimulus was shorter. It is possible that the neurons encoding relative duration specifically in the matching-to-sample task not only reflect the monkeys’ (incorrect and inappropriate) use of timing information in that task (green circles in Fig. 5), but also counteract the influence of each other, as well as other cells contributing to the error (red circles in Fig. 5).

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DISCLOSURES

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AUTHOR CONTRIBUTIONS


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